Postoperative Sepsis: *

Trends and Factors Influencing Sepsis Over a 20-Year Period Reviewed in 20,000 Cases

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THIS REPORT is the final summation and interpretation of four previous studies [1-4] directed to the documentation and analysis of certain features of postoperative sepsis. The four basic reports presented details of methods and results in connection with individual surgical procedures, and our present task is to abstract data and statements to permit a definition of generalizations and conclusions common to all. Our reasons for undertaking this study are several.

The unanswered criticisms of rampant hospital sepsis casually asserted by the lay press as well as by some doctors, the ill-defined impression of the limitation of antibiotics in the prevention and treatment of certain types of surgical sepsis, the avalanche of clinical reports without any statistical control reporting to show trends in sepsis rates, and the convincing reports of certain pediatric and maternity units of epidemic staphylococcal sepsis urged us to undertake an intensive study of postoperative sepsis on a general surgical service. No similar project reviewing over 20 years of clinical experience and limited to a few standard operations has been undertaken at this institution or elsewhere to our knowledge. Specifically, answers were sought for these questions:

1. What is the incidence of postoperative sepsis following a few typical operations?

2. Is there any trend in the incidence of postoperative sepsis over a 20-year period in these same operations?

3. Has the use of whole blood and plasma or the introduction of antibiotics altered the incidence of postoperative sepsis?

4. In these operations is the staphylococcus more prevalent today in postoperative sepsis than formerly?

Previous Studies

Numerous studies have evaluated postoperative sepsis, but because of the complexity of the problem, some reports have limitations which prevent meaningful interpretation. Some overlook the necessity of rigorous statistical control to discriminate between the random effects of chance and relevant clinical factors determining the incidence of postoperative sepsis.[5, 13, 32, 41, 42] Other reports bulk together widely diversified surgical experience so that conclusions in regard to sepsis rates may be confounded by alterations in the case material from time to time.[7, 11, 16, 33, 39] Such changes will affect calculated sepsis rates by the inclusion of various cases in different periods

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with greater or lesser propensities to develop postoperative sepsis. Commonly a precise definition of surgical sepsis or the details as to the methods employed with appropriate checks are omitted. The reader is unable then to interpret the results with any confidence. These frequent limitations of previous studies are not listed in criticism, but rather to emphasize the difficulty in providing hard data on the incidence of postoperative sepsis.

The low incidence of postoperative sepsis following clean surgery, in the order of one to five per cent, requires that many cases be collected to permit meaningful interpretation of the statistics. The complex interdependence of the factors contributing to the development of postoperative sepsis makes it extremely difficult to extract any one factor as the critical one among several hundred that could be responsible for a change in the incidence. These basic problems are difficult to resolve in the analysis of results, and although the present report has its own shortcomings, it may in some measure avoid certain of the disadvantages of the past. Doubtless the future will see further refinements particularly in regard to the availability of critically needed bacteriological data.

Methods

Direct Estimate of Clinical Sepsis. The direct estimate of clinical sepsis has much to commend it for the surgeon inasmuch as we are treating patients and not bacterial counts in the environment. By direct estimate we refer to the accumulation of data on the manifestations of sepsis in the patient in contrast to the indirect technics that define a septic hazzard on the basis of the presence of bacteria in the patient's environment. There is an astonishing difference between the number of reports published on technics designed to reduce the bacterial count in the environment of a surgical patient and the number of reports proving the influence of these methods on the actual manifestations of clinical sepsis. The latter are so uncommon that it might appear they are superfluous.

Such is emphatically not the case. Although the widely-known work of able surgeons and bacteriologist in the past 90 years has repeatedly demonstrated the remarkable achievements of aseptic technics, the data are lacking that define the quantitative relationship of environmental bacterial counts to the development of a septic complication. This important link will be hard to come by, and no one today can say what is the effect on surgical healing of reducing the bacterial population in the operating rooms below that achieved by the application of conventional and rather standardized aseptic technics. Until such quantitative data are at hand, as well as a far more complete understanding of the genesis of postoperative sepsis, it must be accepted that the basic measure of such sepsis, and of means to decrease it, remains the incidence of septic complications in the patient. For these reasons the direct estimate of clinical sepsis, tedious and awkward as it may be, will continue to be important.

Record Survey. The record reviews consisted of a retrospective survey by a team of surgeons and nurses. The nurses were carefully trained and coached in regard to the interpretation of the hospital records with which they were entirely familiar from their clinical work in the hospital. Simple abstracts were completed on every case listing appropriate data enabling a subsequent classification of the records. The operative findings, pathologic report, use of drains, antibiotics, complications, and other relevant details were abstracted. The team of surgeons checked in detail all records that suggested in any way a septic complication at the time of the survey by the nurses. All drained incisions were reviewed as well as all secondary closures. Records that were ambiguous or of doubtful interpretation to the nurses were likewise seen.

The surgeons also checked several hundred records chosen at random to evaluate the consistency and accuracy of the nurses' interpretation. These random checks were satisfactory and gave us complete confidence in the results of the preliminary review by the nursing staff.

Teaching Hospital Facilities. Full advantage was taken of the records at a teaching hospital where medical students, residents, nurses and senior staff jointly maintain unusually complete ones. The student interest in the minutia of wound healing on teaching services results in frequent and informative progress notes. The therapy with antibiotics as well as other medication is part of the permanent hospital record. The diagnostic files and operative files of the hospital record room were particularly helpful in completing the lists of cases without omissions that introduce bias. For our purposes the facts obtained could hardly have been set forth better in the hospital records if the cases had been part of a planned study.

Definition of Sepsis—Minor Sepsis. An inflammation of the abdominal wall incision of unusual degree requiring local or systemic treatment or associated with a febrile response or leukocytosis or prolonged hospitalization. Except for the most trivial of reactions all that were localized around skin sutures or through-and-through sutures were placed in this category. Drainage or positive cultures were not requirements for minor sepsis.

Major Sepsis. An inflammation of the abdominal wall incision or peritoneal cavity, or both, associated with spontaneous or surgically induced purulent drainage greater than a few drops. Intra-abdominal inflammatory masses and abscesses, when diagnosed clinically and even when external drainage was not apparent, were considered major sepsis. Positive cultures were not a requirement for this category.

Assessment of the Influence of Antibiotics. The assessment of the influence of antibiotics was done in two different ways. In those operations where the use of antibiotics was clearly on a so-called "prophylactic" basis it was possible to obtain large groups of cases that were similar in every important respect except for the use of antibiotics. The varying opinions of the staff concerning the indications for their use permitted the comparison of essentially similar cases which were operated upon at about the same time in the hospital. The group not using antibiotics had no treatment with antibiotics or only after the development of a septic complication. The group using "prophylactic" antibiotics started therapy immediately preoperatively, during the operation, or in the immediate postoperative period and continued it for at least four days. Cases that had the antibiotics prescribed intermittently, in inadequate doses, or had the antibiotics started several days before or after the operation were omitted from such comparisons.

A second method was employed following operations for the treatment of appendicitis. In this condition the use of antibiotics is obviously more common in the unfavorable case. Consequently, it was not possible to identify strictly comparable groups of cases that were treated at about the same period to permit a comparison relevant to the use of antibiotics. Therefore, a comparison was made of the results of treatment in appendicitis considering similar cases before and after their introduction. The results of the period 1940–1945 were compared with those of the period 1946–1959 during which antibiotics were used in virtually all the clinically unfavorable cases of appendicitis.

Generally accepted doses, routes, and schedules of administration of the following drugs were used in the cases investigated: penicillin, streptomycin, chlortetracycline, oxytetracycline, tetracycline, chloramphenicol, and erythromycin. It should be clearly understood that the purpose of this part of the review was to determine the effective-

ness of antibiotics as they had been used, not to explore novel methods of use outside the common experience in clinical surgery.

Selection of Cases. Special care was taken in the case selection for study to eliminate confusing and irrelevant influences such as concomitant bowel resections with hysterectomies, colotomies in conjunction with gastric resections, clotting deficits in patients with liver disease, prior radiation therapy of an operative area, an active focus of infection such as osteomyelitis, associated systemic diseases known to lower resistance to infection such as leukemia or pemphigus, and many other problems of similar significance. This deliberate selection results in highly uniform groups of cases for study. The cases removed from consideration clearly had a different risk of sepsis by virtue of some concomitant technical procedure or medical disorder. This winnowing process is essential in obtaining a large and homogenous surgical experience more suitable for comparison from year to year of the incidence of postoperative sepsis. Since it is low, the inclusion of a few septic cases, which properly belong to a different surgical experience, can distort the determined incidence of sepsis.

Justification of Methods. The above methods in their application should provide evidence of their accuracy and precision to justify confidence in the results obtained. There are several features of the study which give assurance of reliability. In the first place the information in the records was well standardized and of uniformly good quality. There was only a handful of records that had to be discarded because of incomplete information. It was evident from the progress notes that the hospital staff was extremely conscientious in recording details of the patients' convalescence. Secondly, the rates of sepsis established varied in different operative procedures in a logical manner. This is perhaps best seen in the stepwise increase in the rates of postoperative sepsis as the pathological stage of acute appendicitis advances. Thirdly, the described check of hundreds of records selected at random revealed no significant disagreement between the initial survey by the nurses and the review by the surgeons.

Finally, the established uniformity of surgical practice throughout the hospital eliminated a variable for which compensation would have been difficult or impossible. There is no reason to suppose that variations in operative technics account for the results in this report. This is not to deny the extreme importance of meticulous surgical technic in reducing postoperative sepsis. However, the uniform quality of operative technic in the four operations considered during the 20-odd years covered by this review does not allow us to invoke technical factors in explaining the significant trends noted.

Operations Studied. Of the four operations chosen for study two were selected because they were essentially elective operations for benign disease. Abdominal hysterectomies were performed in healthy patients of the menopausal age, and inguinal herniorrhaphies were done predominantly in healthy men of all ages. These two operations were almost invariably done at a time of election when all circumstances were propitious for prompt recovery and rarely required whole blood transfusions. Abdominal hysterectomies for malignant disease or for acute pelvic inflammatory disease were excluded from consideration because of the dissimilar procedures indicated depending on the nature of the pathology.

A third operation, subtotal gasterctomy, was selected because it represents a more severe stress to the patient and is a procedure that commonly benefits from whole blood replacement. These important differences from the first two operations reviewed suggested that our understanding of postoperative sepsis would be extended. In the interest of standardizing the surgical ma-

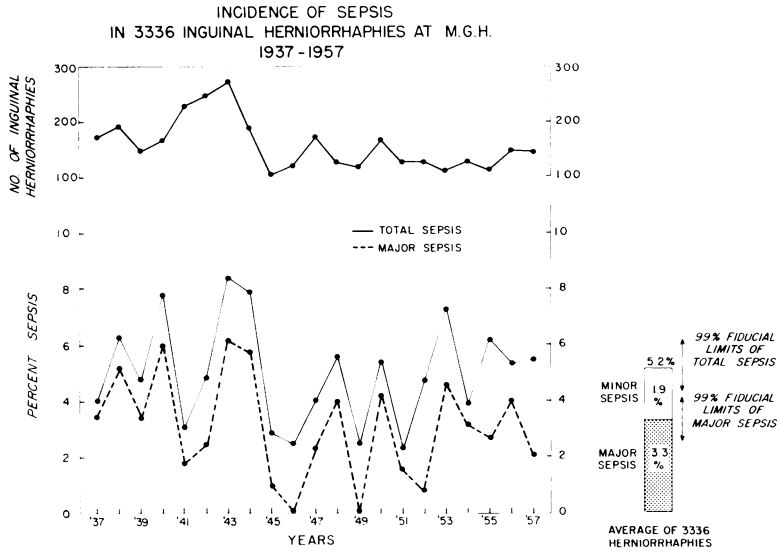

FIG. 1.

terial gastric surgery for bleeding esophageal varies, for lesions requiring a proximal subtotal gastrectomy, or for conditions other than primary gastric disease were not considered. However, emergency gastrectomies for gastroduodenal hemorrhage were included, and in retrospect they formed a special group where massive blood loss, its replacement, operative surgery, and anesthesia placed a unique stress on the patient significantly increasing the risk of postoperative sepsis.

In contrast to these three operations representative of clean surgery appendectomy for acute appendicitis was reviewed as an example of surgery applied to the treatment of a grossly septic process. The cases clearly had to be classified and analyzed in separate groups since the gross pathology noted at the time of the surgical procedure varied from a normal appendix to an appendiceal abscess. The classification defined five groups: Group A—normal appendix removed in conjunction with an exploratory laparotomy for some minor procedure such as an oöphorectomy or a biopsy; Group B—inflamed but not gangrenous appendix; Group C—gangrenous but not perforated appendix; Group D—perforated appendix; and Group E—a group that had developed an appendiceal abscess of sufficient size and involvement where the initial treatment was incision and drainage or a period of conservative management prior to some type of operation. These groups are designated by the first five letters of the alphabet.

Results

Operations with Constant Incidence of Postoperative Sepsis. In those procedures sufficiently numerous the annual rates of sepsis were calculated. The data [1] on the herniorrhaphy study of 3,340 cases is used as an example and is presented in Figure 1. Here the rate of 5.2 per cent for total sepsis

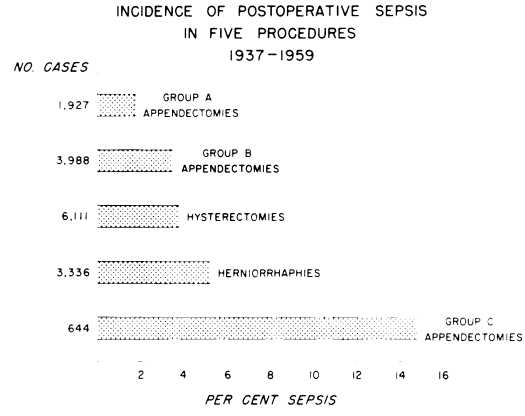

FIG. 2.

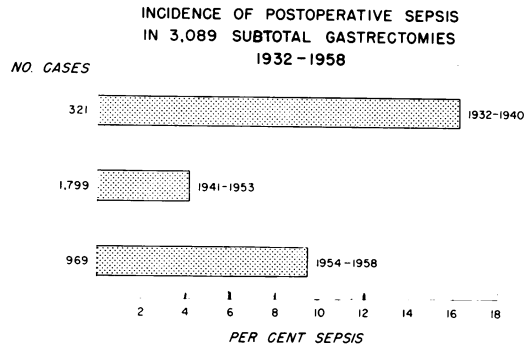

FIG. 3.

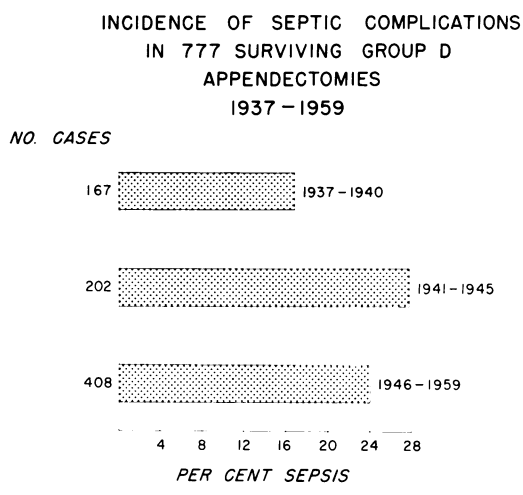

FIG. 4.

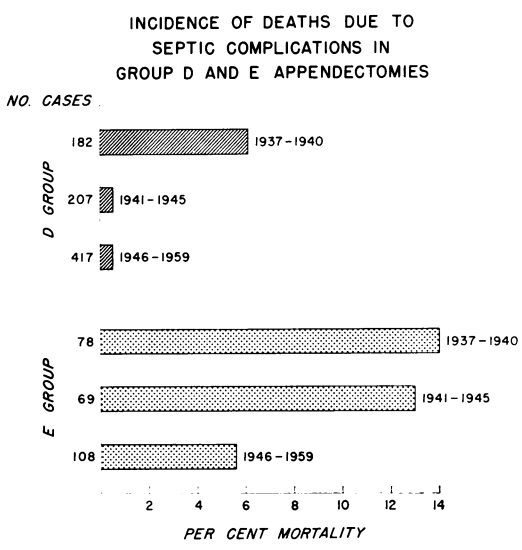

FIG. 5.

is the value for the entire 21-year period about which the individual yearly values fluctuate in a random manner. This is entirely consistent with the assumption that each year represents a random sample from a larger surgical experience characterized by a uniform risk of developing postoperative sepsis of 5.2 per cent. In Figure 2 are displayed the over all incidence of postoperative sepsis in Groups A and B appendectomies, hysterectomies, herniorrhaphies, and Group C appendectomies. Statistical testing indicates these rates are significantly different ($P < 0.001$) and that within each operation they have been constant over the period of this study as discussed in detail for the herniorrhaphies.[1, 3, 4] This experience involving 16,000 operations over a 20-year period provides no evidence of any trend upwards or downwards in the incidence of sepsis following these procedures. The order of increasing risk of developing a septic complication postoperatively in these five procedures is in accord with clinical impressions. The soft tissue dissection during a herniorrhaphy probably accounts for the greater incidence of septic complications than that seen following the hysterectomies. The age of the patient is not a factor here since age-specific rates in Figure 7 show the same difference. The Group C appendectomies, gangrene without perforation of the appendix, understandably have the highest incidence of these complications.

Operations with an Altered Incidence of Postoperative Sepsis. In contrast to the above operations stand the results following subtotal gastrectomies. In Figure 3 are displayed the results recording the postoperative sepsis in three periods: 1) pre-blood bank era (1932–40); 2) post-blood bank era (1941–53); and 3) a period in which indications were distinctly broadened for subtotal gastrectomies (1954–1958). The startling and almost forgotten incidence of septic complications of 16 per cent in the pre-blood bank era fell sharply in the immediate years following the establishment

of a hospital blood bank to the value of 4.1 per cent. No other significant feature of patient care changed abruptly at that time in regard to the indications for or management of subtotal gastrectomies. In particular sulfa drugs were not used routinely and were generally reserved for a septic complication emerging in the postoperative period. The value of 4.1 per cent is lower than the incidence in the last five years reviewed. However, careful scrutiny of the records reveals that the indications for a subtotal gastrectomy have been considerably enlarged to control effectively a lethal gastroduodenal hemorrhage in these recent years. Also during this period a change in hospital policy for the admission of cases to the emergency ward resulted in more emergency bleeders entering for treatment. If these emergency cases are isolated, a significantly higher rate of postoperative sepsis is seen. A large proportion of the recent rise is due to the appearance of such cases in the clinical material. It is not possible to deny categorically the existence of other factors contributing to this rise; however, it is apparent from reviewing all commonly recognized factors pertaining to the incidence of postoperative sepsis that the expanding indications for subtotal gastrectomy to manage acute gastroduodenal hemorrhage have played a major role. This increase was more pronounced on the general service of the hospital where the larger share of the emergency ward patients were admitted. Furthermore, this rise also occurred at a time when those operations listed in Figure 2 had stable rates of postoperative infection. This fact is not in harmony with an interpretation which suggests the rise in the gastrectomy sepsis was part of a trend affecting all operations such as a change in the environmental bacteria. Statistical testing of these differences in the subtotal gastrectomy series indicates they are highly significant ($P < 0.001$).

Considering the remaining operations with an altered incidence of postoperative

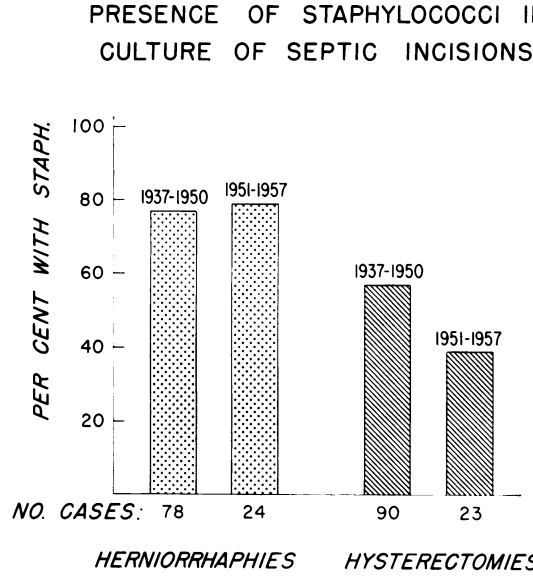

FIG. 6.

sepsis Figures 4 and 5 present data on the Groups D (with perforation) and E (with abscess formation) of the appendectomy study. The rates of postoperative sepsis in Group D survivors are in Figure 4. The mortality rates in the Group D and E cases due to a septic complication are in Figure 5. In these figures the cases have been segregated into groups representing the pre-

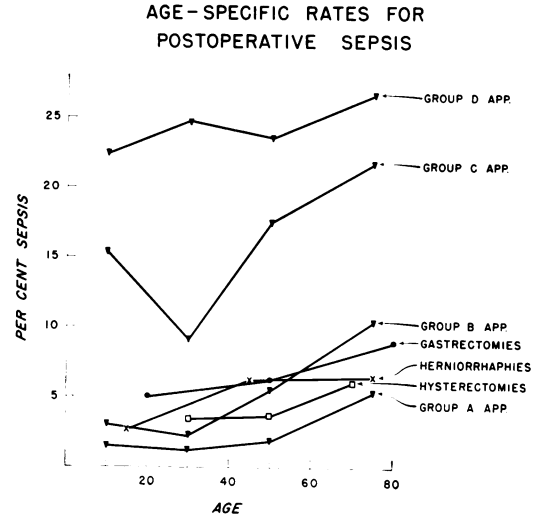

FIG. 7.

blood bank and pre-antibiotic era (1937–1940), the post-blood bank and pre-antibiotic era (1941–1945), and the post-blood bank and post-antibiotic era (1946–1959). In Figure 4 the unexpected increase in postoperative sepsis from 16.8 to 25.2 per cent for the last two periods taken together is noted after the establishment of the hospital blood bank ($0.02 < P < 0.05$). This result is presumably due to the more effective means of treating the cardiovascular collapse of peritonitis favoring the ultimate survival of many cases with a perforated appendix that previously perished. These precarious survivors remained alive to develop septic complications.

Confirmation for this interpretation is seen in Figure 5 where the mortality due to septic complications declines sharply from 6.1 to 0.48 per cent in Group D after the start of the blood bank ($P < 0.001$). This drop is about the same as the increase in incidence of septic complications seen in Group D survivors after the establishment of the blood bank. In Group E the blood bank facilities apparently were not associated with any change in the incidence of mortality due to septic complications. However, following the introduction of antibiotics, in 1946, the mortality rate dropped from 14 to 5.6 per cent ($P < 0.001$). This is very reasonably a consequence of the antibiotics reducing the tendency of the septic process to spread directly or by way of the lymphatics and blood vessels and to cause ultimately a septic death.

In the years following 1940, the sulfa drugs were used extensively in the treatment of peritonitis, and in this study of appendicitis it has been impossible to separate the contemporaneous influence of the use of whole blood, plasma, and sulfa drugs. An interpretation placing greater weight on the effects of these drugs cannot be denied. However, the significant decline in the incidence of postoperative sepsis following subtotal gastrectomies in 1940, and maintained in subsequent years, is one example where the blood bank facilities were associated with an improvement separate from the routine prescription of sulfa drugs.

Influence of Antibiotics. In considering the influence of antibiotics a series of comparisons were made within Group A appendectomies, hysterectomies, herniorrhaphies, and gastrectomies establishing paired groups. As stated under methods these groups were entirely similar save for the use of antibiotics on a "prophylactic" basis. The number of cases in these comparisons totals over 11,000, and there is not any evidence to suggest that the rate of postoperative sepsis has been altered by the antibiotics employed in the conventional ways stipulated in the section on methods. The documentation for this has been presented in detail.[2-4]

In considering the influence of antibiotics in the B-, C- and D-group appendectomies it was not possible to match contemporaneous surgical experience for the reasons discussed under the section on methods. However, the comparison before and after the introduction of antibiotics is presented for Group D in Figure 4. The constancy of the incidence of sepsis in this comparison as well as the constancy seen in Groups B and C as commented upon in the discussion of Figure 2 are against the antibiotics having a detectable beneficial effect in the over all results in these cases. However, we have no means of proving or disproving that in a few instances, too small numerically to affect the over all results, their use was of critical importance. To ferret out these cases would require far more information about all the contributing factors entering into the decision to use antibiotics than the hospital records convey. Here the intuitive art of clinical management is important and elusive to the medical statistician.

Incidence of Staphylococcal Infections. Bacteriologic studies in this retrospective review were not entirely satisfactory. Only those incisions with major sepsis had drain-

age to be cultured, and only the more severe infections were investigated in this manner. Approximately one fifth of the cases after 1951 had been on antibiotics when suppuration developed. The culture technics in general employed aerobic blood agar plates and thioglycollate broth cultures unless some distinctly unusual clinical problem developed. Coagulase tests were not routinely carried out, and phage typing was not available in the years covered by this study.

The data in the herniorrhaphy and hysterectomy studies are displayed in Figure 6. The percentage of the cultured incisions that yielded staphylococci initially are seen for two different periods. The periods compared were those before and after 1951, and this dividing point was chosen since the extensive use of broad spectra antibiotics throughout the hospital in recent years was to be tested for its influence on the balance of bacteria growing in septic incisions. In Figure 6, only modest changes in the incidence of staphylococci in the cultured septic incisions are noted, and these changes with either operation are not statistically significant. Thus there is no evidence in terms of two standard operations that staphylococcal sepsis is absolutely or relatively more frequent.

Age-Specific Rates. A graph of the incidence of sepsis at different ages is displayed in Figure 7 where are collected data from as many operations. The differences in the incidence of sepsis between these various procedures has already been discussed, and the data here permit a review of any correlation with age. Considering each operation separately there is no impressive trend, but collectively there can be little doubt that only a slight increase in the amount of postoperative sepsis emerges as age increases.

Discussion

Table 1 presents a summary of the postoperative sepsis rates established by this report. In considering the data on operations with a constant incidence of postoperative sepsis it is noteworthy that such a large group of standardized cases presents no trend upwards or downwards in the rate of postoperative sepsis over a 20-year period. The conclusion is inescapable that the risk at this hospital of postoperative sepsis, when measured by means of uniform surgical procedures, has been constant during the period of the survey. The aseptic surgical technics practiced yield consistent results in aborting sepsis postoperatively. We must endeavor to improve the stable rates of postoperative sepsis in these operations ranging between 1.0 and 15 per cent. They are similar to the rates established by other studies that give internal evidence of a determined search for all postoperative sepsis using a definition of sepsis roughly comparable to that in this report.[8, 17–21, 23, 30, 43] The differences in these surveys can largely, if not entirely, be explained by dissimilar case material and details in methods. In the survey reported here, although the definition of sepsis may be broadened or restricted by the reader, at least he may review the results of a consistent definition

TABLE 1. *Postoperative Sepsis Rates*

Operation	% Sepsis	Cases Reviewed
Inguinal herniorrhaphy 1937–57	5.2	3,340
Abdominal hysterectomy 1937–57	3.8	6,110
Subtotal gastrectomy:		
1932–1940 Pre-blood bank era	16	320
1941–1953 Post-blood bank	4.1	1,800
1954–1958 Broadened indications for emergency gastrectomy	9.4	970
Appendectomy 1937–1959:		
A Appendix not inflamed	1.7	1,980
B Appendix inflamed	3.5	4,130
C Appendix gangrenous	15	640
D Appendix perforated	25	810
E Appendiceal abscess	Not applicable	250
Totals		20,350

applied to surgical experience over a 20-year period.

Further improvement need not necessarily follow a different use of antibiotics, a restatement of the surgical conscience, a more rigorous aseptic technic, a screening of the operating room staff for asymptomatic carriers of bacteria, institution of measures to reduce further the bacterial density on the surgical wards, and so forth since we have no clear idea as to the genesis of most septic complications. Information is needed in regard to the origin of these complications in the surgical incision. Intimate details of wound healing await clarification.

Some of the major sepsis, and possibly most of the minor sepsis, in this study may be regarded as the end result of suboptimal healing perhaps occasioned initially by such circumstances as the presence of a hematoma, collection of serum in a dead space, reaction to suture material, or ischemic tissue necrosis. If an incision is not healing properly, then the difficulties may ultimately manifest themselves as a septic complication because of the ubiquitous bacteria awaiting their opportunity in virtually all surgical incisions. It has been said that bacteria are a *necessary* but not a *sufficient* condition for the development of incisional sepsis; and if this is agreed upon, it lends equal importance to the definition of those circumstances that permit bacterial growth as well as the definition of those circumstances that result in their presence in overwhelming numbers in the incision. Dubos has clearly stated the case against the concept of specific etiologies in most infectious disease or against the concept that bacteria are a sufficient condition.[10] He has shown how medical thinking is muddled when conclusions are contrived from facts with the misguidance of the *a priori* assumption that a specific etiology exists.

The work of Dubos,[9] Miles and associates [26-28] and of Johnson and associates [14, 15, 22] has emphasized the importance of local and systemic factors that hinder or favor the development of a septic lesion. That similar factors, essentially non-bacterial at their inception, may account for outbreaks of clinical sepsis has received scant attention.

The various reports on the epidemiology of staphylococcal sepsis present illuminating, if conflicting, interpretations [6, 29, 30, 40, 42, 43] and a monograph by Williams and associates [44] is a most helpful guide although unable to accomplish a reconciliation of the reports on this topic. These epidemiologic studies are just beginning to unravel the complex circumstances that result in bacteria appearing in a surgical incision in numbers sufficient to cause trouble. As yet, conclusive data are not available although in certain investigations the correlation of the phage type of the staphylococci in the patient's nose and in his septic surgical incision convinced Williams and associates that "self-infection is important in the etiology of the septic lesions." [43] Why this correlation exists is not clear. Perhaps nose and operative site are infected from a third site on the patient. Possibly transient bacteremias derived from the respiratory tract following intubation for anesthesia are important. Repeated percutaneous injections play an undetermined role in seeding the circulation with skin bacteria. The new evidence at least suggests that the density of environmental bacteria is not so obviously culpable as assumed in the past.

Turning to the operations with a changing incidence of postoperative sepsis a variety of clinically significant factors are associated with these changes. The apparent importance of the blood bank and the restricted role of antibiotics has been demonstrated. Obviously one cannot prove in a retrospective study that a causal relationship exists between a change in the rate of sepsis and some particular feature in the clinical management; all that can be established is a strong likelihood in veiw of the temporal association. Confirmation of the critical importance of whole blood replace-

ment is seen in the experimental work of Miles previously cited and in a series of papers by Fine and associates.[34, 36-38] These studies are in harmony with clinical impressions, and the blood bank appears to be a most important factor in reducing the rate of postoperative sepsis in the gastrectomy series and in reducing the mortality due to sepsis of patients with a perforated appendix from 6 per cent to less than one half per cent. The sulfa drugs may share with the blood bank the responsibility for this decline in mortality in cases with a perforated appendix.

The increase in the last five years in the sepsis rates of subtotal gastrectomies due to the admission of emergency cases illustrates another nonbacterial factor which can complicate the interpretation. The evolution of the indications for an operation, which has so frequently been troublesome in other medical statistics, is a snare in the evaluation of postoperative sepsis. The analysis of the subtotal gastrectomy experience in relation to the use of antibiotics did not indicate that these drugs had been effective in altering the incidence of sepsis of 4.1 per cent during the 1941–1953 era, which statistically was an entirely homogeneous surgical experience in this regard. Consequently, the subtotal gastrectomy experience was not broken for analysis at the end of 1945. These examples demonstrate the importance of not limiting our explanations to superficial, bacterial mechanisms.

The influence of antibiotics has been a subject of intense study, and it is emphasized that we can only discuss the results in terms of the operations selected and in terms of the way the antibiotics were used in this hospital. Beneficial effects in regard to their "prophylacitc" use were not discernible. Of course, it is always possible to claim that if the drugs had been used differently in larger doses, with more frequent injections, starting several days preoperatively, chosen in relation to preoperative skin cultures and sensitivities, etc., a difference would emerge in the healing of a surgical incision. The likelihood of this is remote in the authors' opinion considering the present evidence. All that can be claimed from this study is that in these particular operations the use of antibiotics, as dictated by common hospital practice, exerted no influence or an influence so negligible as not to be discernible by these technics. However, the benefit in reducing the mortality due to sepsis following the development of an appendiceal abscess was clear cut. It has not been possible to define any other group where the use of antibiotics has been helpful in the treatment of appendicitis. This decline in mortality in cases with an abscess clearly justifies their continued use to combat the direct and metastatic extension of the septic process.

In this limited condemnation of the effectiveness of antibiotics, even in the treatment of a septic process such as appendicitis, we realize that there are shortcomings. It is expected that other studies may be designed to circumvent these limitations. However, no matter how the study is designed it seems unlikely that a major influence of antibiotics would emerge reducing septic complications in all stages of appendicitis. Nothing that has been stated here is interpreted as evidence for or against the use of antibotics in other procedures such as cardiac surgery, peripheral vascular surgery, neurosurgery, or in the treatment of extraperitoneal sepsis. A cardinal principle substantiated by this study is that each clinical situation must be tested individually. Other studies have concluded that "prophylactic" antibiotics following certain operations are valueless.[24, 25, 35]

The constant incidence of staphylococci in the septic incisions of hysterectomies and herniorrhaphies refutes the commonly asserted claim that staphylococcal infections are in recent years more prevalent following all operations. The over all figure of 65 per cent representing the incidence of staphylococci in 215 cultured incisions with major

sepsis is virtually the same as the incidence of 60 per cent based on 380 septic wounds reported elsewhere.[30] If such infections appear more common, it is because they complicate types of cases that favor the growth of the staphylococcus. A well-known example of this phenomenon is seen in the emergence of staphylococcal pneumonia in recent years. It has been shown that the use of penicillin by suppression of the competitive pneumococcus has provided the resistent staphylococcus with a highly favorable situation for growth.[12, 31]

In considering the age-specific rates the trends are small with increasing age of the patient. Although in reviewing the operations individually there did not appear to be a statistically impressive trend, it is apparent when collectively reviewed. This would suggest that resistance to postoperative infection is maintained very well in the later decades in life and that the increasing age of the patient population today cannot be invoked to explain any gross difference in the incidence of sepsis. Although age does not emerge here as a striking factor, it is obvious sense that when age is associated with advanced medical disorders that impair resistance such as renal disease or cardiovascular disease, sepsis will be favored. However, the degenerative diseases account for this, not age *per se*.

A plea is made for the evaluation of the hazzards of postoperative sepsis on the basis of its appearance in the patients, the clinical target. The essential bacteriological studies of the surgical environment will assume a new meaning when correlated with the emergence of postoperative sepsis in the patient. The advantage of conducting these studies in large groups of standardized surgical cases may be important for subsequent interpretation. Conventional statistical analyses will be necessary to distinguish the irrelevant effects of chance from those which must enter significantly into our clinical reasoning in the successful care of future patients.

Conclusions

From this review the following conclusions are stated:

1. In each of five standardized surgical procedures there has been a constant incidence of postoperative sepsis over the past 20 years.
2. The determined risk of postoperative sepsis is modified by use of whole blood and plasma, by the selection of case material, and by the proportion of cases included in a study with different, inherent risks of postoperative sepsis.
3. Considering four standardized surgical procedures the "prophylactic" use of antibiotics prescribed in conventional ways did not influence the rate of postoperative sepsis.
4. The beneficial effect of antibiotics in the treatment of appendicitis was only apparent in the decline in mortality due to sepsis in cases forming an appendiceal abscess. The beneficial effects of the availability of whole blood, plasma and sulfa drugs were apparent in the decline in the mortality due to sepsis in cases with a free perforation of the appendix.
5. Considering the incisions that developed sepsis in two standardized surgical procedures there is no increase in the relative proportion of staphylococci present in recent years among other bacteria.
6. For their complete interpretation the enumeration of bacteria in the surgical environment and measures designed to decrease the bacterial population must be correlated with studies establishing the incidence of postoperative sepsis in the patient.
7. Statistical control is essential in studies where we are considering a septic event occurring in a relatively small proportion of the total number of cases.

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